CLINICAL ARTICLE

Long-Term Follow-Up of Multilevel Thoracic Ossification of the Posterior Longitudinal Ligament Following Circumferential Decompression *via* Posterior Approach: A Retrospective Study

Xiao Liu, MD[1,2,3†], Shu-heng Zhai, MD[1,2,3†], Qing-peng Song, MD[1,2,3†], Feng Wei, MD[1,2,3], Liang Jiang, MD[1,2,3], Chui-guo Sun, MD[1,2,3], Xiao-guang Liu, MD[1,2,3], Wei-shi Li, MD[1,2,3]

[1]*Department of Orthopaedics, Peking University Third Hospital,* [2]*Engineering Research Center of Bone and Joint Precision Medicine and* [3]*Beijing Key Laboratory of Spinal Disease Research, Beijing, China*

Objective: To examine the postoperative progression of multilevel thoracic posterior longitudinal ligament (OPLL) at circumferential decompression (CD) levels and evaluate the long-term results after CD *via* the posterior approach.

Methods: Clinical data from 16 patients with thoracic myelopathy secondary to OPLL who underwent CD at a single center were evaluated retrospectively from 2007 to 2014 and were followed up for more than 60 months. Patients of all sexes and ages were included in the study. Thin-slice computed tomography scans obtained at the time of surgery and the most recent follow-up were analyzed. The ossified area was measured on the axial reconstructed scan of the most obvious protrusion of ossification at the CD level. The neurological outcomes were evaluated using modified Japanese Orthopaedic Association (JOA) scores and Hirabayashi recovery rates (HRRs). Continuous variables were presented as the mean ± standard deviation and were analyzed using the Student's *t*-test, while categorical variables were tested using Fisher's exact test.

Results: Among all patients, the most predominant type was the mixed type (9/16, 56.3%), while the circumscribed type was only found in two patients (12.5%), and the continuous type was found in five patients (31.2%). Six cases were associated with ossification of the ligamentum flavum, and two cases were combined with cervical OPLL. The OPLL area at the CD level increased in all patients. The mean follow-up period was 5.5 ± 0.92 years (range 5–8 years). The mean area of ossification increased from 35.63 ± 39.23 mm^2 at the time of surgery to 99.94 ± 65.39 mm^2 at the last follow-up visit ($P < 0.01$). There was no internal fixation disorder on any computed tomography scan after the operation. The average JOA score of all patients improved from 4.2 ± 2.2 points before surgery to 8.4 ± 2.6 points at the final follow-up ($P < 0.01$). The overall HRR was 61.8%. None of the patients exhibited any neurological deterioration due to OPLL progression. One patient developed a severe gait disturbance due to worsening lumbar canal stenosis, an unrelated cause, but the other 15 experienced gait disturbance improvements.

Conclusions: According to the long-term follow-up results, although OPLL progression did not decrease or stop after removing the OPLL mass, CD is a safe and effective procedure that can provide adequate reserve ventral space to cope with postoperative OPLL progression.

Key words: Circumferential decompression; Ossification of the posterior longitudinal ligament; Progression; Thoracic spine

Address for correspondence Wei-shi Li, MD and Xiao-guang Liu, MD, Department of Orthopaedics, Peking University Third Hospital, 49 North Garden Road, Haidian District, Beijing, China 100191 Tel/Fax: +86-13501358705; Email: puh3liweishi@163.com and xglius@vip.sina.com

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†The authors contributed equally to the article.

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Introduction

Ossification of the posterior longitudinal ligament (OPLL) in the thoracic spine causes severe thoracic myelopathy, which is an ectopic ossification of the posterior longitudinal ligament at the thoracic spine with an unknown cause. Imaging examination is a necessary means to diagnose OPLL. The imaging morphology can be divided into localized, continuous, segmental, and mixed types. OPLL can result in a reduced spinal canal and foraminal volume, compression of the spinal cord or nerve roots, and spinal cord injury and nerve root irritation symptoms. It progresses slowly, has a low incidence, and can cause thoracic spinal stenosis with a high disability rate. A recent study reported that the prevalence of thoracic OPLL (T-OPLL) in Japanese patients is 1.6%[1,2]. The most common symptoms of upper T-OPLL are lower extremity numbness, lower extremity weakness, and gait instability, while lower T-OPLL usually manifests as conus spinal cord syndrome or cauda equina syndrome. However, most patients with T-OPLL have no obvious symptoms, and surgical treatment is the only option. Different surgical approaches have been reported previously with the continuous development of surgical techniques and medical instruments, including the anterior approach, posterior approach, combined anterior and posterior approach, and circumferential decompression (CD) *via* the posterior approach[3–5]. The common outcomes of surgery for multilevel thoracic myelopathy caused by T-OPLL may be unfavorable because of the anatomical features of the thoracic spine and high operation risk for thoracic surgeries. Complications such as aggravation of symptoms, cerebrospinal fluid leakage, and infection often occur after surgery. The outcomes of thoracic surgery are closely related to the surgeon's experience, such as careful performance. T-OPLL seems to be one of the most challenging diseases in spinal surgery, and no consensus has been reached regarding the optimal timing for operations and surgical procedures[6].

A large T-OPLL mass can lead to severe spinal cord compression, and it is difficult to obtain an ideal decompression effect by anterior or posterior decompression alone. Therefore, CD can be considered. CD *via* the posterior approach is an emerging option, removing the ventral dural compressive elements directly and enlarging the spinal canal, but long-term results of this approach are lacking[7]. Compared with traditional surgery, posterior CD for bilateral pedicle resection has a wider field of vision, improves the safety of the operation, and does not need to enter the thoracic cavity. Moreover, it can reduce the incidence of complications in anterior surgery. It has been proven to be an effective and safe surgical procedure with a fair final neurologic recovery postoperatively.

There is still the possibility of disease recurrence after CD *via* the posterior approach, regardless of the completion of decompression. Previous studies reported that progression of cervical OPLL was more common in patients who received surgical treatment than in patients who did not undergo surgical treatment because of biological stimulation after decompression, such as changes in the microcirculatory environment within the spinal canal. Histological studies of OPLL have shown that the development of OPLL is a process of endochondral ossification, beginning with the differentiation of mesenchymal stem cells into chondrocytes. Several studies have revealed that cervical OPLL progresses after surgery[8–10]. However, information concerning the progression of multilevel T-OPLL is lacking. In addition, the long-term results of CD are unclear. In addition, there are a variety of surgical methods for T-OPLL, but the choice of different surgical methods is still controversial due to high technical requirements and high risks. The purposes of this study are as follows: first, to evaluate the long-term surgical outcomes in patients with T-OPLL after CD *via* the posterior approach, including clinical characteristics, the course of neurologic recovery, improvements in gait disturbance, and surgical safety; second, to examine the postoperative progression of CD levels of multilevel T-OPLL in a long-term follow-up and evaluate the long-term results after CD *via* the posterior approach; and third, to explore the mechanism of ossification progression.

Methods

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (i) patients diagnosed with T-OPLL; (ii) T-OPLL involving three vertebral segments or more; (iii) patients that underwent OPLL extirpation through CD *via* the posterior approach; (iv) initial computed tomography (CT) scan and subsequent follow-up CT scans were performed using the same protocol, with the latest CT scan at least 24 months after the first CT scan.

The exclusion criteria were as follows: (i) patients with a history of trauma; (ii) CT scan with different protocols.

Ethical Approval

This study was approved by the ethics committee of our hospital's institutional review board. Written informed consent was obtained from all patients whose specimens and clinical information were used for this study.

Selection and Description of the Participants

We retrospectively reviewed 16 patients with symptomatic multilevel T-OPLL who underwent CD *via* the posterior approach in the orthopaedic department of our hospital from 2007 to 2014. All patients underwent radiological examinations, including plain radiography, CT, and magnetic resonance imaging. T-OPLL was diagnosed based on clinical and radiological evidence by at least two experienced spinal surgeons. Patients who were followed up for more than 60 months were included in the analysis. According to the standard follow-up protocol, thoracic CT scans of multilevel T-OPLL patients were performed every 2 to 3 years after surgery.

Measurement of Ossification/Radiographic Assessment

The progression of the T-OPLL mass was compared between the initial CT scan obtained at discharge and the CT scan obtained at the last follow-up. The CT scans were obtained with a slice thickness of 0.3 mm. The data were transferred *via* a Digital Imaging and Communications in Medicine network to a GE computer workstation using the GE Healthcare Centricity RIS CE V3.0/PACS software program. We reconstructed the CT scans for 3D multiplanar reconstruction. Sagittal reconstruction was used to determine the thoracic spine level with the most severe ossification protrusion, number of involved segments, and types of ossification. We measured the area of ossification in the axial reconstruction parallel to the endplate of the corresponding vertebra. Three blinded observers, including two spinal surgeons and one radiologist, independently performed the measurements. All CT measurements were obtained twice at an interval of 2 weeks by two independent raters.

Surgical Procedures

The surgical procedures for CD *via* the posterior approach were similar to those reported by Liu *et al.*[11].

Anesthesia and position (step 1): Patients lay prone on the operative table. General anesthesia was administered, and intraoperative electrophysiological monitoring was used.

Approach and exposure (step 2): First, the posterior elements of the spine, including the spinous process, lamina, and facet joints of the involved segments (as well as at least two more segments above and below the area), were fully exposed through a midline incision. Pedicle screws were then implanted at one level above and below the involved segments.

Intraoperative findings and resection (step 3): The spinous process was removed, and gutters were made along the midline of the facet joint of both sides with a high-speed drill. Subsequently, en bloc laminectomy was performed. After posterior decompression was completed, we observed refilling and pulsating of the dural sac and conducted intraoperative ultrasonography to check for any residual ventral spinal compression. If there was suspicion or evidence of sufficient ventral decompression, which was caused by the poor shifting of the thoracic spinal canal or the presence of a "beak-shaped" OPLL protruding into the spinal cord, these levels were marked out for additional CD. CD was performed *via* a transpedicular approach, and the bilateral residual facets and pedicles were resected with a high-speed drill and curette. The posterior third of the vertebral cancellous bone was removed to make a "cave" at the levels requiring ventral decompression. Finally, the posterior vertebral cortex and the ossified posterior longitudinal ligament were carefully pressed to collapse, and the ossified posterior longitudinal ligament was resected to achieve complete ventral decompression. If it is impossible to respect the ossified posterior longitudinal ligament from the ossified dural sac, parts of the dura mater were meticulously exfoliated. A real-time assessment of residual ventral compression after CD was performed again to ascertain decompression sufficiency.

Fixation and reconstruction (step 4): Titanium rods of an appropriate length were selected and connected to each screw. After moderate pressure, these were tightened and fixed. The cut spinous process and lamina were crushed and placed outside the articular process, and the wound was closed after washing, hemostasis, and checking.

Neurological Assessment

Neurological status and surgical outcomes were assessed using the modified Japanese Orthopaedic Association (JOA) scoring system for thoracic myelopathy on admission, at discharge, and the last follow-up. The Japanese Orthopaedic Association's evaluation of treatment scores is mainly used to evaluate human functional disorders. The JOA score system includes four sections: upper limb motor function (4 points), lower limb motor function (4 points), sensation (6 points), and bladder function (3 points). The overall JOA score was 29 points at the highest level and zero points at the lowest level, with lower scores indicating greater spinal cord dysfunction. The Hirabayashi recovery rate (HRR) was calculated to assess final neurologic recovery. HRR is equal to (postoperative JOA value – preoperative JOA value)/(17 – preoperative JOA value) × 100% (excellent [100%–75%], good [74%–50%], fair [49%–10%], unchanged [9%–0%], and worse [<0])[3].

Statistical Analysis

Statistical analyses were performed using SPSS Statistics (version 23.0; IBM Corp. Released 2015. IBM SPSS Statistics for Windows, version 23.0. Armonk, NY: IBM Corp.). Data for continuous variables are presented as the mean ± standard deviation. The differences between different follow-up times were analyzed using the Student's *t*-test. Fisher's exact test was used to identify differences between the categorical variables. Statistical significance was defined at a *P*-value of <0.05 based on two-tailed tests.

Results

Demographic Characteristic

The population included five males and 11 females with a mean age of 58.5 ± 8.7 years (range 37–66 years). The mean follow-up period was 5.5 ± 0.92 years (range 5–8 years).

Radiological analysis of OPLL in the thoracic spine revealed three subtypes: continuous, circumscribed, and mixed. Among them, the most predominant type was the mixed type (9/16, 56.3%), while the circumscribed type was only found in two patients (12.5%). The continuous type was found in five patients (31.2%). The level of T-OPLL, extension of OPLL, surgical areas of decompression and fixation, number of CD, and follow-up periods are shown in Table 1. The distribution of the T-OPLL is shown in Fig. 1. The co-occurrence of ossification of the ligamentum flavum (OLF)

TABLE 1 Demographic and surgical information of patients

No. of patients	Age/ (years)	Sex	Type of T-OPLL	Preop-Extension of OPLL	Surgical level			Area of T-OPLL (mm^2)		JOA score		Follow-up (yrs)	HRR (%)
					Decompression	Fixation	CD level	Postop	Last FU	Pre	Last FU		
1	41	M	Continuous	T_{2-6}	T2–T6	T3–T8	T5/6	32.3	166.3	2	10	6.5	88.9
2	45	F	Mixed	T_{1-8}	T3–T8	T3–T9	T6/7	0	253.6	5	11	7	100.0
3	52	M	Continuous	T_{2-7}	T2–T6	T2–T6	T4/5	40.8	51.5	3	8	8	62.5
4	61	M	Continuous	T_{1-3}	C7–T3	C6–T3	T1/2	50.2	86.7	3	11	5	100
5	41	F	Mixed	T_{4-8}, T_{11-12}	T5–8	T5–8	T5/6	47	81.7	8	11	6	100
6	43	M	Mixed	T_{1-2}, T_{3-12}	T8–T12	T8–L1	T9/10, T10/11	42.6 0	67 136.1	0	11	5	100
7	47	M	Mixed	T_{2-3}, T_{5-9}	T5–T9	T5–10	T6/7, T7/8	56.2 0	88.3 21.5	4	4	5	0
8	37	F	Mixed	T_{3-10}	T3–T10	T3–10	T4/5, T5/6, T6/7	70.5 80.3 81.5	128.7 117.8 130.3	4	9	5	71.4
9	63	F	Circumscribed	T_{5-7}	T_5–T_7	T_{4-9}	$T_{5/6}$, $T_{6/7}$	0 0	69.7 65.7	4	7	5	42.9
10	66	F	Circumscribed	T_{2-3}, T_{5-6}	T_{1-6}	T_{1-6}	$T_{2/3}$	0	59.2	5	5	5	0
11	61	F	Mixed	T_{1-3}, T_{11-12}	T_{1-6}	T_{1-6}	$T_{1/2}$	0	72.9	1	10	5	90.0
12	50	F	Mixed	T_{1-8}, T_{11-12}	C_6–T_5	C_6–T_5	$T_{2/3}$	143.4	264.7	5	7	5	33.3
13	45	F	Mixed	T_{1-4}, T_{6-8}	T_{1-4}	T_{1-4}	$T_{2/3}$	28.6	32	5	11	5	100.0
14	51	F	Continuous	T_{1-7}	T_{1-4}	T_{1-4}	$T_{2/3}$	0	30.4	4	5	5	14.3
15	48	F	Continuous	T_{1-7}	T_{1-6}	T_{1-6}	$T_{2/3}$	0	52.0	4	5	5	14.3
16	47	F	Mixed	T_{4-7}, T_{11-12}	T_{3-7}	T_{3-7}	$T_{5/6}$	71.8	122.6	9	10	6	50.0
Mean ± SD								35.63 ± 39.23	99.94 ± 65.39	4.2 ± 2.2	8.4 ± 2.6		61.8

The average area of ossification was 35.63 ± 39.23 mm^2 preoperatively and 99.94 ± 65.39 mm^2 at the last follow-up ($P < 0.001$).; Progression rate = area at the time of surgery/area at the last follow-up visit, the average progression rate = 280.5.; CD, circumferential decompression; HRR: Hirabayashi recovery rates; JOA: modified Japanese Orthopaedic Association; Postop, area of ossification at the time of surgery; Preop-Extension of OPLL, preoperative extension of OPLL; SD, standard deviation; T-OPLL, thoracic ossification of the posterior longitudinal ligament.

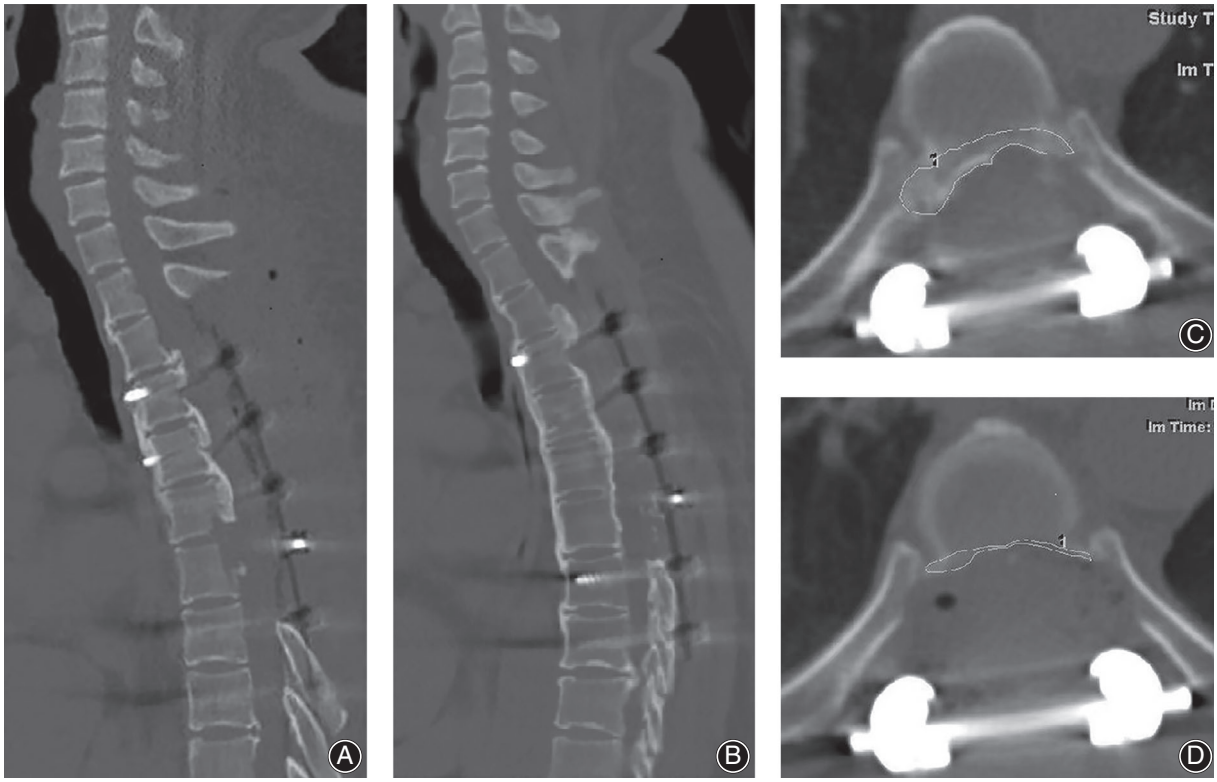

Fig. 1 Level and area of the ossification. (A) Sagittal section postoperatively. The arrow referred to the circumferential decompression (CD) level. (B) Sagittal section at the last follow-up time. The arrow referred to ossification progression at the CD level. (C) Axial section postoperatively. It showed ossification was excised completely at the CD level. (D) Axial section at the last follow-up time. It showed ossification progression at the CD level.

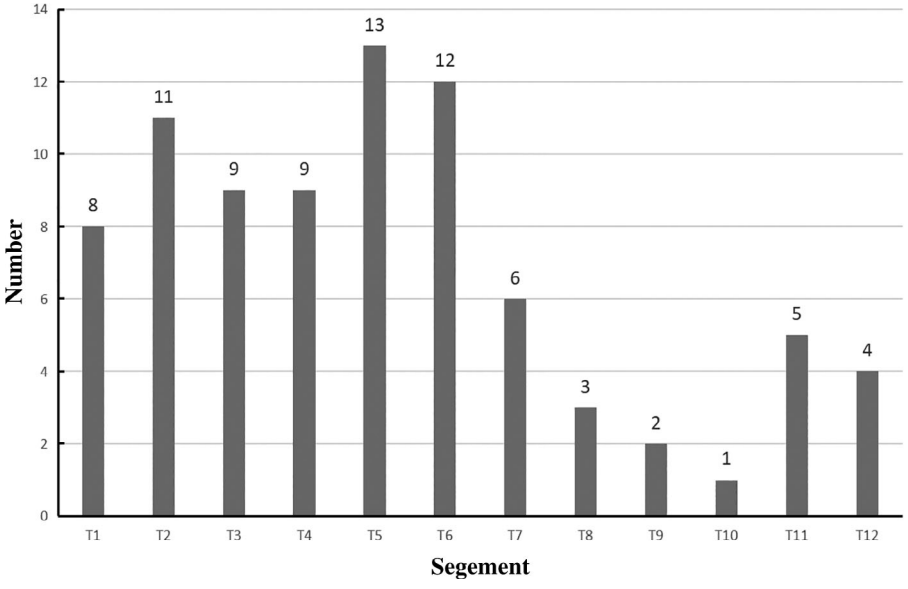

Fig. 2 Distribution and characteristics of T-OPLL in this study.

in the affected segment was observed in six cases, accounting for 37.5% of all cases. The two cases with combined cervical OPLL accounted for 12.5% of all cases.

OPLL Progression

There were 21 segments of OPLL observed in 16 patients who were followed up for more than 5 years. The OPLL area increased in all patients (Table 1 and Fig. 2). The average area of ossification was 35.63 ± 39.23 mm^2 preoperatively and 99.94 ± 65.39 mm^2 at the last follow-up ($P < 0.001$). All areas of ossification increased in both width and thickness, and the average area increased by 180.5%. Nine of the patients with no previous ossification at the time of surgery had severe ossification at the last follow-up visit. The most common segment of OPLL progression was $T_{2/3}$, followed by $T_{6/7}$. OPLL progression was more obvious in $T_{2/3}$ and $T_{6/7}$. Screw loosening and rod breakage were not observed on any of the follow-up postoperative CT scans.

Courses of Neurologic Recovery

The mean thoracic JOA score was 4.2 ± 2.2 before surgery and 8.4 ± 2.6 at the most recent follow-up visit ($P < 0.001$) (Table 1). The mean HRR was 61.8%. None of the patients exhibited neurological deterioration due to OPLL progression. One patient developed a severe gait disturbance due to an unrelated cause (worsening of lumbar canal stenosis), but the other 15 experienced gait disturbance improvements.

Complications

No definite complications were observed during or after the operation.

Discussion

Surgical Effect and Clinical Characteristics

In the present study, we investigated the postoperative progression of T-OPLL and evaluated the long-term results after CD using the posterior approach. This 5-year follow-up study indicated that the length and width of the maximum region of ossification in patients with T-OPLL still tend to increase after total resection by CD. We also found that although T-OPLL progressed, all patients achieved a satisfactory recovery at the last follow-up, and no patients exhibited any neurological deterioration due to T-OPLL progression.

T-OPLL is an ectopic ossification of the posterior longitudinal ligament at the thoracic spine with an unknown cause and is one of the leading causes of thoracic myelopathy. OPLL is most prevalent in East Asians, especially in Japanese, South Koreas, and Chinese. Although T-OPLL is less common than cervical OPLL, it has an insidious onset, high disability rate, high surgical risk, and high postoperative paralysis rate[12]. CD is a promising but invasive surgical approach, removing the compressive force directly. Nevertheless, the long-term results of this approach are unclear. Progression of cervical OPLL has been well-documented in the literature. However, the progression of T-OPLL remains to be elucidated.

Ossification Progression

Multiple studies have indicated that cervical OPLL progression is common. Yoshimura *et al.* showed that cervical OPLL progressed in all affected subjects in a group of 30 patients after a follow-up of 3 years[8]. Byung-wan *et al.* evaluated the progression of 60 patients with cervical OPLL by CT with a minimum follow-up of 2 years and found that progression of cervical OPLL is associated with younger age, involvement of multiple levels, and mixed type morphology[13]. One study reported the progression of T-OPLL after posterior compression and fixation. Shurei *et al.* analyzed nine consecutive patients with T-OPLL who underwent posterior decompression and fixation for at least 3 years of follow-up and concluded that the size of the T-OPLL still increased after spinal stabilization[14].

This study is among the first to investigate the progression of T-OPLL after CD. In the present study, most T-OPLL cases were of continuous and mixed types. In addition, progression of T-OPLL was observed in all cases after more than 5 years follow-up. Previous studies have shown that progression is more frequent in patients with continuous and mixed types of cervical OPLL. This was, to some extent, in accordance with previous studies. However, it depends on whether CD was performed. Further studies are required that examine whether continuous and mixed types of T-OPLL are more common.

Mechanism Research

To date, the etiology and pathomechanism of OPLL remain unclear. Multiple studies have suggested that OPLL is a multifactorial disease influenced by numerous genetic and non-genetic factors[15,16]. Non-genetic factors include mechanical stress, degeneration process, diet, and biological rhythm. Compared to the cervical spine, the thoracic spine has a smaller range of motion limited by the thorax. It is universally acknowledged that the thoracic spine is more stable, experiences less mechanical stress than the cervical spine, and is less susceptible to degeneration. Genetic studies of T-OPLL revealed that deleterious mutations in several genes might contribute to the development of T-OPLL by whole genome sequencing.

Previous studies reported that progression of cervical OPLL was much more common in patients who had undergone surgical treatment than in those who received nonsurgical treatment due to biological stimulation after decompression, such as changes in the microcirculatory environment within the spinal canal. Histological studies of OPLL suggest that OPLL develops through the process of endochondral ossification, initiating from the differentiation of mesenchymal stem cells into chondrocytes. In most of the studies on the progression of cervical OPLL and T-OPLL, the surgical patterns were decompression and stabilization *via* a posterior procedure. T-OPLL continues to grow after

spinal stabilization because the OPLL mass still exists after surgery. However, in the current study, all T-OPLL masses were completely resected by CD. As a result, we speculated that the following factors caused progression. First, the OPLL mass was not completely removed, and the remnant of the OPLL mass progressed postoperatively. Second, after the OPLL was resected, there were changes in the microcirculatory environment within the spinal canal. The mechanism of progression of OPLL is similar to that of myositis ossificans traumatica. Third, the adjacent longitudinal ligament continued to gradually expand into the original site.

The security and efficacy of CD have been discussed in several previous studies. Multiple studies have reported that CD is a safe and effective procedure[3,7]. However, there are debates regarding indications for CD. Lee *et al.* advocated that CD through a posterior approach is safe, effective, and less invasive to ventral dural compressive lesions in the lower thoracic region[17]. Ma *et al.* retrospectively investigated the clinical outcomes of 23 patients with T-OPLL circumferential spinal cord decompression and concluded that indications of CD are limited to thoracic myelopathy caused by severe anterior impingement of various etiologies from T_4–T_{12}[18]. The results of this study are highly reliable because it has the longest follow-up time to date in evaluating the long-term results of patients with T-OPLL after CD. Although T-OPLL progressed in all affected subjects in our study, myelopathy was not influenced by the progression in the current 5-year follow-up study. CD can provide adequate reserve ventral space to cope with postoperative T-OPLL progression. In the present study, CD was performed in seven patients in the upper thoracic spine. All patients recovered well after long-term follow-up. We considered that the outcomes of thoracic surgery are closely related to the surgeon's experience, such as careful performance.

There are several limitations to this study. First, the number of patients enrolled was relatively small. A multicenter study with a larger sample size should be performed to examine T-OPLL. Second, the measurement process was semi-automatic. Therefore, human errors may have occurred. However, we believe that the evaluation of the ossification area was accurate and valid, as indicated by the high intra-observer and inter-observer intra-class correlation coefficients. Third, the follow-up duration was short. T-OPLL progression may result in neurological dysfunction after a longer follow-up period. Our findings need to be fully proven over a more prolonged follow-up period.

In conclusion, the present study demonstrated that the size of the T-OPLL increased after CD. Although the OPLL mass was mostly removed at the CD level, OPLL progression did not decrease or stop. According to the long-term follow-up results, CD is a safe and effective procedure that can provide adequate reserve ventral space to cope with postoperative OPLL progression.

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Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Xiao Liu, Shu-heng Zhai, Qing-peng Song, Feng Wei, Liang Jiang, and Chui-guo Sun. The first draft of the manuscript was written by Xiao Liu, Shu-heng Zhai, and Qing-peng Song. Xiao-guang Liu and Wei-shi Li revised the manuscript.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee for Human Subjects of the Peking University Third Hospital and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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